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09/692,412	10/20/2000	David F. Bush	04983.0206.CPUS01/38-21(1	6988

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EXAMINER

EINSMANN, JULIET CAROLINE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/692,412

Applicant(s)

BUSH ET AL.

Examiner

Juliet C Einsmann

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 July 2002 and 10 December 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,10-12,15-17 and 27-35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,10,11,15-17 and 27-35 is/are rejected.
- 7) ☒ Claim(s) 12 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 7/24/02 and 12/10/02, papers numbered 13 and 15. The claims have not been amended. Claims 1-7, 10-12, 15-17, and 27-35 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 4, 6, 17, 29, 30, 31, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho *et al.* (Nature Genetics, 1999, 23:203-207) in view of Lai *et al.* (Genomics, 54:31-38, 1998).

Cho *et al.* teach a method of identifying a region of genomic DNA associated with a phenotypic trait of interest comprising:

(A) screening a mapping population of Arabidopsis plants to determine the linkage of said phenotypic trait with a collection of nucleic acid molecules, wherein said nucleic acid molecules are capable of detecting a set of polymorphisms, where the polymorphisms are distributed throughout the genome of said mapping population of Arabidopsis;

(B) calculating the linkage of each of said polymorphisms to said phenotypic trait; and
(C) identifying said genomic DNA region associated with said phenotypic trait based on its linkage to one or more of said nucleic acid molecules (p. 205, third column).

The set of polymorphisms screened by Cho *et al.* included the polymorphism instantly disclosed as Single Nucleotide Polymorphism 466799 (confirmed in Applicant's remarks filed 11/16/01, page 8). The region of genomic DNA associated with said phenotypic trait is located within 7cM region between two single nucleotide polymorphisms (SNP), thus it is about 5cM from at least one of the polymorphisms.

Cho *et al.* suggest the generation of denser SNP maps for Arabidopsis (p. 205), but Cho *et al.* do not teach a method wherein the polymorphisms are distributed throughout the genome of Arabidopsis plants at an average density of more than one polymorphism per about 100 kb.

Lai *et al.* teach a high density SNP map of a portion of the human genome, wherein the map has a density of one SNP every 30 kb, and teach that such a map was generated "efficiently and rapidly" using existing methodologies (p. 34).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods taught by Lai *et al.* in order to produce a denser SNP map for use in the identification of a region of genomic DNA associated with a phenotypic trait of interest as taught by Cho *et al.* The ordinary practitioner would have been motivated to provide such a method by the suggestion of Cho *et al.* that "The generation of denser biallelic maps should allow high-throughput identification of both monogenic and polygenic traits, effectively removing the rate-limiting nature of high resolution mapping from the study of biological processes (p. 205)." The ordinary practitioner would have been further

motivated by the teachings of Lai *et al.* that the generation of SNP-based maps can be accomplished "efficiently and rapidly" using existing methodologies.

4. Claims 1-3, 5, 10-11, 15-16, 27, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho *et al.* in view of Lai *et al.* as applied to claims 4, 6, 17, 29, 30, 31, 33, and 34 above, and further in view of Davis *et al.* (PNAS, Vol. 96, pp. 6541-6546, May 1999).

The teachings of Cho *et al.* in view of Lai *et al.* are applied to these claims as discussed in the previous rejections.

While the methods taught by Cho *et al.* and Lai *et al.* are both directed towards use in positional cloning, Cho *et al.* in view of Lai *et al.* do not teach a method in which the region of genomic DNA is isolated. Steps (A)-(D) are inherent properties of the generation of an F2 generation of plants as taught by Cho *et al.* Cho *et al.* generate the F2 generation from two different ecotypes of Arabidopsis wherein one ecotype has a phenotype of interest and the other ecotype lacks the phenotype of interest (p. 205).

Davis *et al.* teach methods in which positional cloning is used to localize and isolate a region of genomic DNA associated with a phenotype of interest (p. 6542).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included a step in which the methods of Cho *et al.* in view of Lai *et al.* are used to isolate the region of genomic DNA that is associated with the phenotype. The ordinary practitioner would have been motivated to isolate the region of genomic DNA the isolation of genomic DNA of interest aids in the elucidation of the biochemical pathways that lead to a particular phenotype. For example, Davis *et al.* teach that the availability of genes in

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the pathway they are examining "should be instrumental in defining the synthetic defects" mutant plants (p. 6546).

5. Claims 1-7, 10-11, 15-17, and 27-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho *et al.* (Nature Genetics, 1999, 23:203-207) in view of Somerville (posted to bionet.genome.arabidopsis USENET newsgroup (May 2000)).

Cho *et al.* teach a method of identifying a region of genomic DNA associated with a phenotypic trait of interest comprising:

(A) screening a mapping population of Arabidopsis plants to determine the linkage of said phenotypic trait with a collection of nucleic acid molecules, wherein said nucleic acid molecules are capable of detecting a set of polymorphisms, where the polymorphisms are distributed throughout the genome of said mapping population of Arabidopsis;

(B) calculating the linkage of each of said polymorphisms to said phenotypic trait; and

(C) identifying said genomic DNA region associated with said phenotypic trait based on its linkage to one or more of said nucleic acid molecules (p. 205, third column).

The set of polymorphisms screened by Cho *et al.* included the polymorphism instantly disclosed as Single Nucleotide Polymorphism 466799 (confirmed in Applicant's remarks filed 11/16/01, page 8). The region of genomic DNA associated with said phenotypic trait is located within 7cM region between two single nucleotide polymorphisms (SNP), thus it is about 5cM from at least one of the polymorphisms. Steps (A)-(D) are inherent properties of the generation of an F2 generation of plants as taught by Cho *et al.* Cho *et al.* generate the F2 generation from

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two different ecotypes of Arabidopsis wherein one ecotype has a phenotype of interest and the other ecotype lacks the phenotype of interest (p. 205).

Cho *et al.* suggest the generation of denser SNP maps for Arabidopsis (p. 205), but Cho *et al.* do not teach a method wherein the polymorphisms are distributed throughout the genome of Arabidopsis plants at an average density of more than one polymorphism per about 100 kb.

Somerville discloses the availability of a dataset that represents more than 35,000 polymorphisms in the Arabidopsis genome, and provides instructions as to how to access the database for use in “the isolation of genes in map based cloning, among other things.”

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the denser SNP map taught by Somerville in the identification of a region of genomic DNA associated with a phenotypic trait of interest as taught by Cho *et al.* The ordinary practitioner would have been motivated to provide such a method by the suggestion of Cho *et al.* that “The generation of denser biallelic maps should allow high-throughput identification of both monogenic and polygenic traits, effectively removing the rate-limiting nature of high resolution mapping from the study of biological processes (p. 205),” and Somerville provides such a method. The ordinary practitioner would have been further motivated by the teachings of Somerville that “This is an incredible resource – no other organism has such a rich collection of polymorphisms. Obviously, this will greatly facilitate the isolation of genes by map based cloning.”

Response to Remarks

The rejection are reiterated from the previous office action.

With regard to the rejection set forth over *Cho et al.* in view of *Lai et al.*, applicant argues that the deficiencies of *Cho et al.* are not overcome by *Lai et al.* because *Lai et al.* is not discussing the Arabidopsis genome. Applicant's argument, however, fails to consider the rejection as a whole. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is true that *Lai et al.* are not dealing with the Arabidopsis genome, the examiner does not assert as much. But, *Lai et al.* are dealing with an analogous problem in humans, that is the production of sets of polymorphisms that are useful in methodologies for detecting genes associated with traits. *Cho et al.* specifically motivate one to produce denser biallelic maps, and *Lai et al.* teach that the production of such maps is possible using standard techniques. These combined teachings would have motivated the one of ordinary skill in the art to have undertaken the production of denser biallelic maps for the Arabidopsis genome as suggested by *Cho et al.* Thus, the rejection is maintained.

Applicant's remarks with respect to claim 12 are persuasive and therefore claim 12 is not rejected in view of *Cho et al.* in view of *Lai et al.* and further in view of *Davis et al.*

With regard to the rejection set forth over *Cho et al.* in view of *Somerville et al.*, applicant argues that *Somerville* does not actually disclose the dataset, nor do they teach a method wherein the polymorphisms are distributed throughout the genome of Arabidopsis plants at an average density of one polymorphism per about 100kb. However, this is not a persuasive argument because *Somerville et al.* do provide enabling disclosure of how to access the database

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by teaching that the database exists and directing users as to how to access it. Somerville further provides a clear suggestion to use the database in such methods. In order to have a set of polymorphisms that is distributed an average every 100kb throughout the Arabidopsis genome only 1000 markers would be needed. The dataset referred to by Somerville has 35,000 markers, and thus has an average density of more than 1 per every 100kb of the Arabidopsis genome. Thus, the rejection is maintained.

In view of Applicant's response to the request for information, this rejection is withdrawn with regard to claim 12 since the polymorphism 471736 was not in the database at the time Somerville *et al.* provided the posting to the usenet group.

Conclusion

6. No claims are allowed.
7. Claim 12 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

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organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Juliet C Einsmann
Examiner
Art Unit 163434

February 22, 2003



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